

1. An isolated nucleic acid molecule comprising a sequence of nucleotides derived from a eukaryotic chromosome and encompassing a neocentromere or a functional derivative synthetic or hybrid form thereof which nucleic acid molecule or its derivatives, synthetic forms or hybrid forms when introduced into a compatible cell is capable of replicating, acting as an extra-chromosomal element and segregating with cell division.

3. An isolated nucleic acid molecule according to claim 3 wherein the chromosome is a human chromosome.

5. An isolated nucleic acid molecule according to claim 4 wherein the chromosome is human chromosome 10 or a modified form of human chromosome 10 or its non-human mammalian or non-mammalian equivalent.

6. An isolated nucleic acid molecule according to claim 5 wherein the nucleotide sequence corresponds to a region mapping between q24 and q26 on chromosome 10.

7. An isolated nucleic acid molecule according to claim 5 wherein a modified form of human chromosome 10 is a mardel (10) chromosome.

8. An isolated nucleic acid molecule according to claim 6 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 3 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 3 under low

-126-

stringency conditions at 42°C.

9. An isolated nucleic acid molecule according to claim 7 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 4 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 4 under low stringency conditions at 42°C.

10. An isolated nucleic acid molecule according to claim 7 comprising a nucleotide sequence substantially as set forth in one or more of SEQ ID NOs: 5-29 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to one or more of SEQ ID NOs: 5-29 under low stringency conditions at 42°C.

11. An isolated nucleic acid molecule according to claim 1 wherein the length of the nucleic acid molecule is from about 50 bp to about 1500 kbp.

12. An isolated nucleic acid molecule according to claim 11 wherein the length of the nucleic acid molecule is from about 1 kbp to about 1000 kbp.

13. An isolated nucleic acid molecule according to claim 12 wherein the length of the nucleic acid molecule is from about 10 kbp to about 500 kbp.

14. An isolated nucleic acid molecule according to claim 13 wherein the length of the nucleic acid molecule is from about 10 kbp to about 100 kbp.

15. An isolated nucleic acid molecule comprising a nucleotide sequence encompassing a neocentromere or a functional derivative, synthetic or hybrid form thereof which when said nucleic acid molecule is in linear form and co-introduced into a cell together with a telomeric sequence, is capable of replicating, remaining as an extra-chromosomal element and segregates with cell division.

16. An isolated nucleic acid molecule according to claim 15 wherein the nucleotide sequence

-127-

is derived from a mammalian chromosome.

17. An isolated nucleic acid molecule according to claim 16 wherein said nucleic acid molecule is capable of associating with CENP-A and CENP-C antibodies.

18. An isolated nucleic acid molecule according to claim 16 or 17 wherein the mammalian chromosome is human chromosome 10 or a modified form of chromosome 10 or its non-human mammalian or non-mammalian equivalent.

19. An isolated nucleic acid molecule according to claim 18 wherein the nucleotide sequence corresponds to a region mapping between q24 and q26 on chromosome 10.

20. An isolated nucleic acid molecule according to claim 18 wherein the modified form of human chromosome 10 is mardel (10) chromosome.

21. An isolated nucleic acid molecule according to claim 18 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 3 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 3 under low stringency conditions at 42°C.

22. An isolated nucleic acid molecule according to claim 19 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 4 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 4 under low stringency conditions at 42°C.

23. An isolated nucleic acid molecule according to claim 19 comprising a nucleotide sequence substantially as set forth in one or more of SEQ ID Nos: 5-29 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to one or more of SEQ ID Nos: 5-29 under low stringency conditions at 42°C.

24. An isolated nucleic acid molecule according to claim 15 wherein the length of the nucleic

-128-

acid molecule is from about 50 bp to about 1500 kbp.

25. An isolated nucleic acid molecule according to claim 24 wherein the length of the nucleic acid molecule is from about 1 kbp to about 1000 kbp.

26. An isolated nucleic acid molecule according to claim 25 wherein the length of the nucleic acid molecule is from about 10 kbp to about 500 kbp.

27. An isolated nucleic acid molecule according to claim 26 wherein the length of the nucleic acid molecule is from about 10 kbp to about 100 kbp.

28. An isolated nucleic acid molecule or its chemical equivalent encompassing a human neocentromere or a functional derivative thereof or a latent, synthetic, hybrid or its mammalian or non-mammalian homologue.

29. An isolated nucleic acid molecule according to claim 28 wherein said nucleic acid molecule when introduced into a compatible cell is a replicating, extra-chromosomal element which segregates with cell division.

30. An isolated nucleic acid molecule according to claim 29 wherein the nucleic acid molecule is capable of associating with centromeric binding proteins (CENP)-A and -C or antibodies thereto.

31. An isolated nucleic acid molecule according to claim 29 or 30 wherein the chromosome is human chromosome 10 or a modified form of human chromosome 10 or its non-human mammalian or non-mammalian equivalent.

32. An isolated nucleic acid molecule according to claim 31 wherein the nucleotide sequence corresponds to a region mapping between q24 and q26 on chromosome 10.

33. An isolated nucleic acid molecule according to claim 31 wherein a modified form of

-129-

human chromosome 10 is a mardel (10) chromosome.

34. An isolated nucleic acid molecule according to claim 31 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 3 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 3 under low stringency conditions at 42°C.

35. An isolated nucleic acid molecule according to claim 32 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 4 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 4 under low stringency conditions at 42°C.

36. An isolated nucleic acid molecule according to claim 32 comprising a nucleotide sequence substantially as set forth in one or more of SEQ ID Nos: 5-29 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to one or more of SEQ ID Nos: 5-29 under low stringency conditions at 42°C.

37. An isolated nucleic acid molecule according to claim 28 wherein the length of the nucleic acid molecule is from about 50 bp to about 1500 kbp.

38. An isolated nucleic acid molecule according to claim 37 wherein the length of the nucleic acid molecule is from about 1 kbp to about 1000 kbp.

39. An isolated nucleic acid molecule according to claim 38 wherein the length of the nucleic acid molecule is from about 10 kbp to about 500 kbp.

40. A genetic construct comprising an origin of replication for a eukaryotic cell and a nucleic acid molecule encompassing a eukaryotic neocentromere or a functional derivative thereof or a latent, synthetic, hybrid form thereof or its mammalian or non-mammalian homologue flanked by telomeric nucleotide sequences functional in the cell in which the genetic construct is to replicate and wherein said genetic construct when introduced into a cell is a replicating, extra-

-130-

chromosomal element which segregates with cell division.

41. A genetic construct according to claim 40 wherein the eukaryotic neocentromere is a mammalian centromere.
42. An isolated nucleic acid molecule according to claim 41 wherein the neocentromere is a human neocentromere.
43. An isolated nucleic acid molecule according to claim 42 wherein the nucleic acid molecule is capable of associating with CENP-A and -C or antibodies thereto.
44. An isolated nucleic acid molecule according to claim 43 wherein the neocentromere is from human chromosome 10 or a modified form of human chromosome 10 or its non-human mammalian or non-mammalian equivalent.
45. An isolated nucleic acid molecule according to claim 44 wherein the human neocentromere maps to a region between q24 and q26 on chromosome 10.
46. An isolated nucleic acid molecule according to claim 44 wherein a modified form of human chromosome 10 is a mardel (10) chromosome.
47. An isolated nucleic acid molecule according to claim 45 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 3 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 3 under low stringency conditions at 42°C.
48. An isolated nucleic acid molecule according to claim 46 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 4 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 4 under low stringency conditions at 42°C.

-131-

49. An isolated nucleic acid molecule according to claim 46 comprising a nucleotide sequence substantially as set forth in one or more of SEQ ID Nos: 5-29 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to one or more of SEQ ID Nos: 5-29 under low stringency conditions at 42°C.

50. An artificial chromosome for use in gene therapy said artificial chromosome comprising a nucleic acid molecule capable of conferring a phenotypic property on a cell carrying said artificial chromosome wherein said artificial chromosome is a replicating element which segregates with cell division.

51. An artificial chromosome according to claim 50 wherein said artificial chromosome is capable of functioning in a mammalian cell.

52. An artificial chromosome according to claim 51 wherein said artificial chromosome is capable of functioning in a human cell.

53. An artificial chromosome according to claim 52 wherein the chromosome is a human chromosome.

54. An artificial chromosome according to claim 53 wherein the chromosome is capable of associating with CENP-A and -C or antibodies thereto.

55. An artificial chromosome according to claim 53 or 54 wherein the chromosome is human chromosome 10 or a modified form of human chromosome 10 or its non-human mammalian or non-mammalian equivalent.

56. An artificial chromosome according to claim 55 comprising a region mapping between q24 and q26 on chromosome 10.

57. An artificial chromosome according to claim 5 wherein a modified form of human chromosome 10 is a mardel (10) chromosome.

-132-

58. An artificial chromosome according to claim 56 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 3 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 3 under low stringency conditions at 42°C.

59. An artificial chromosome according to claim 57 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 4 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 4 under low stringency conditions at 42°C.

60. An artificial chromosome according to claim 57 comprising a nucleotide sequence substantially as set forth in one or more of SEQ ID Nos: 5-29 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to one or more of SEQ ID Nos: 5-29 under low stringency conditions at 42°C.

61. An isolated nucleic acid molecule comprising a sequence of nucleotides which defines a eukaryotic neocentromere.

62. An isolated nucleic acid molecule according to claim 61 wherein the neocentromere is derived from a mammalian chromosome.

63. An isolated nucleic acid molecule according to claim 61 wherein the neocentromere is derived from a human chromosome.

64. An isolated nucleic acid molecule according to claim 63 wherein the nucleic acid molecule is capable of associating with centromeric binding proteins (CENP)-A and -C or antibodies thereto.

65. An isolated acid molecule according to claim 63 or 64 wherein the chromosome is human chromosome 10 or a modified form of human chromosome 10 or its non-human mammalian or non-mammalian equivalent.



66. An isolated nucleic acid molecule according to claim 65 wherein the nucleotide sequence corresponds to a region mapping between q24 and q26 on chromosome 10.
67. An isolated nucleic acid molecule according to claim 65 wherein a modified form of human chromosome 10 is a mardel (10) chromosome.
68. An isolated nucleic acid molecule according to claim 66 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 3 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 3 under low stringency conditions at 42°C.
69. An isolated nucleic acid molecule according to claim 67 comprising a nucleotide sequence substantially as set forth in SEQ ID NO: 4 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to SEQ ID NO: 4 under low stringency conditions at 42°C.
70. An isolated nucleic acid molecule according to claim 67 comprising a nucleotide sequence substantially as set forth in one or more of SEQ ID NOs: 5-29 or a nucleotide sequence having at least 40% similarity thereto or a nucleotide sequence capable of hybridising to one or more of SEQ ID NOs: 5-29 under low stringency conditions at 42°C.
71. An isolated nucleic acid molecule according to claim 61 wherein the length of the nucleic acid molecule is from about 50 bp to about 1500 kbp.
72. An isolated nucleic acid molecule according to claim 71 wherein the length of the nucleic acid molecule is from about 1 kbp to about 1000 kbp.
73. An isolated nucleic acid molecule according to claim 72 wherein the length of the nucleic acid molecule is from about 10 kbp to about 500 kbp.
74. An isolated nucleic acid molecule according to claim 73 wherein the length of the nucleic

191

[illegible]